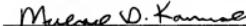




<b>TRANSMISSION LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371</b>		ATTORNEY'S DOCKET NUMBER <b>040283-0213</b>
INTERNATIONAL APPLICATION NO. PCT/GB2003/003168	INTERNATIONAL FILING DATE 7/24/2003	U.S. APPLICATION NO. (if known, see 37 C.F.R. 1.5) <b>10/522,873</b>
PRIORITY DATE CLAIMED <b>8/2/2002</b>		
TITLE OF INVENTION <b>SUBSTITUTED THIENYL-HYDROXAMIC ACIDS AS HISTONE DEACETYLASE INHIBITORS</b>		
APPLICANT(S) FOR DO/EO/US Janet Ann ARCHER et al.		
Applicant hereby submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:		
<ol style="list-style-type: none"> <li><input type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a filing under 35 U.S.C. 371.</li> <li><input checked="" type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. 371.</li> <li><input type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.</li> <li><input type="checkbox"/> The US has been elected (Article 31).</li> <li><input type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2))           <ul style="list-style-type: none"> <li><input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau).</li> <li><input type="checkbox"/> has been communicated by the International Bureau.</li> <li><input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US)</li> </ul> </li> <li><input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2))           <ul style="list-style-type: none"> <li><input type="checkbox"/> is attached hereto.</li> <li><input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4).</li> </ul> </li> <li><input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))           <ul style="list-style-type: none"> <li><input type="checkbox"/> are attached hereto (required only if not transmitted by the International Bureau).</li> <li><input type="checkbox"/> have been communicated by the International Bureau.</li> <li><input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li> <li><input type="checkbox"/> have not been made and will not be made.</li> </ul> </li> <li><input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).</li> <li><input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</li> <li><input type="checkbox"/> An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</li> </ol>		
Items 11 to 20 below concern other document(s) or information included:		
<ol style="list-style-type: none"> <li><input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98 (2 pages); PTO Form SB08 (3 pages) and copies of 39 of 42 listed references.</li> <li><input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</li> <li><input type="checkbox"/> A preliminary amendment.</li> <li><input type="checkbox"/> An Application Data Sheet under 37 CFR 1.76.</li> <li><input type="checkbox"/> A substitute specification.</li> <li><input type="checkbox"/> A power of attorney and/or change of address letter.</li> <li><input type="checkbox"/> A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821 – 1.825</li> <li><input type="checkbox"/> A second copy of the published international application under 35 U.S.C. 154(d)(4).</li> <li><input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).</li> <li><input type="checkbox"/> Other items or information:</li> </ol>		

U.S. APPLICATION NO. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
10/522,873	PCT/GB2003/003168	040283-0213
The following fees have been submitted:		
21. <input checked="" type="checkbox"/> Basic national fee	\$300	\$ 300.00
22. <input checked="" type="checkbox"/> Examination fee		
If International preliminary examination report prepared by USPTO and all claims satisfy provisions of PCT Article 33(1)-(4)		
All other situations		
23. <input checked="" type="checkbox"/> Search fee		
Search fee (37 CFR 1.445(e)(2)) has been paid on the international application to the USPTO as an International Searching Authority		
International Search Report prepared and provided to the Office		
All other situations		
<b>TOTAL OF ABOVE 21, 22 and 23 =</b>		
<input checked="" type="checkbox"/> Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$ for each additional 50 sheets of paper or fraction thereof.		
Total Sheets	Extra sheets	Number of each additional 50 or fraction thereof (round up to a whole number)
214 - 100 = 114	/50 =	3
x \$250.00		
\$ 750.00		
Surcharge of \$130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 CFR 1.492(e))		
\$ 0.00		
CLAIMS	NUMBER FILED	NUMBER EXTRA
Total Claims	33 - 20 =	13
x \$ 50.00		
\$ 650.00		
Independent Claims	1 - 3 =	0
x \$ 200.00		
\$ 0.00		
MULTIPLE DEPENDENT CLAIM(S) (if applicable)		
+ \$ 360.00		
\$		
<b>TOTAL OF ABOVE CALCULATIONS =</b>		
\$ 2400.00		
<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. Fees above are reduced by ½.		
<b>SUBTOTAL =</b>		
\$ 2400.00		
Processing fee of 130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(i)).		
\$		
<b>TOTAL NATIONAL FEE =</b>		
\$ 2400.00		
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). 40.00 per property		
\$		
<b>TOTAL FEES PREVIOUSLY PAID =</b>		
\$ 2400.00		
<input type="checkbox"/> <b>Amount to be refunded:</b> <input type="checkbox"/> <b>charged:</b>		
a. <input type="checkbox"/> A check in the amount of _____ to cover the above fees is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. 19-0741 in the amount of _____ to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 19-0741. A duplicate copy of this sheet is enclosed. d. <input type="checkbox"/> Fees are to be charge to a credit card. <b>WARNING:</b> Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.		
NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the International Application to pending status.		
SEND ALL CORRESPONDENCE TO:		
Foley & Lardner LLP Customer Number: 22428		
 SIGNATURE Michael D. Kaminski NAME 32,904 REGISTRATION NUMBER		

May 6, 2005

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Janet Ann ARCHER et al.

Title: SUBSTITUTED THIENYL-HYDROXAMIC ACIDS AS  
HISTONE DEACETYLASE INHIBITORS

Appl. No.: 10/522,873

Filing Date: 2/2/2005

Examiner: Unassigned

Art Unit: Unassigned

**INFORMATION DISCLOSURE STATEMENT**  
**UNDER 37 CFR §1.56**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Submitted herewith on Form PTO/SB/08 is a listing of documents known to  
Applicants in order to comply with Applicants' duty of disclosure pursuant to 37 CFR §1.56.

A copy of each non-U.S. patent document and each non-patent document is being  
submitted to comply with the provisions of 37 CFR §1.97 and §1.98.

The submission of any document herewith, which is not a statutory bar, is not  
intended as an admission that such document constitutes prior art against the claims of the  
present application or that such document is considered material to patentability as defined in  
37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be  
appropriate to antedate or otherwise remove as a competent reference any document which is  
determined to be a *prima facie* art reference against the claims of the present application.

**TIMING OF THE DISCLOSURE**

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

**RELEVANCE OF EACH DOCUMENT**

An English translation of the foreign-language documents A23 and A26 is not readily available. Document A23 discloses psammoplakin analogues of chlamydocin and Document A26 discloses simple aryl thienylhydroxamic acids. English abstracts are provided with foreign-language documents A7, A8, A10 and A20. The absence of English-language translations does not relieve the PTO from its duty to consider the submitted foreign language documents (37 CFR §1.98 and MPEP §609).

Applicants respectfully request that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

Date May 6, 2005

By Michael D. Kaminski

FOLEY & LARDNER LLP  
Customer Number: 22428  
Telephone: (202) 672-5490  
Facsimile: (202) 672-5399

Michael D. Kaminski  
Attorney for Applicant  
Registration No. 32,904

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INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

Date Submitted: May 6, 2005

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Sheet

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of 3

## Complete if Known

Application Number	10/522,873
Filing Date	2/2/2005
First Named Inventor	Janet Ann ARCHER
Group Art Unit	Unassigned
Examiner Name	Unassigned
Attorney Docket Number	040283-0213

## U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
B1	2002-0065282	A1		Georges et al.	05/30/2002	
B2	5,369,108			Breslow et al.	11/29/1994	
B3	5,922,837			Meinke et al.	07/13/1999	

## FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document		Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)			
B4	EP	0 847 992		A1	Mitsui Chemicals, Inc.	06/17/1998	
B5	EP	1 216 984		A1	Beacon Laboratories, Inc.	06/26/2002	
B6	EP	1 216 986		A2	Beacon Laboratories, Inc.	06/26/2002	
B7	JP	11-302173		A	Mitsui Chemicals, Inc.	11/02/1999	A
B8	JP	11-335375		A	Mitsui Chemicals, Inc.	12/07/1999	A
B9	WO	98/00127			RAPHAELI, Ada	01/08/1998	
B10	WO	99/11659			Japan Energy Corporation	03/11/1999	A
B11	WO	00/08048			Fujisawa Pharmaceutical Co., Ltd.	02/17/2000	
B12	WO	00/38322		A1	Methylgene, Inc.	05/31/2001	
B13	WO	01/70675		A2	Methylgene, Inc.	09/27/2001	
B14	WO	02/22577		A2	Novartis-Erfindungen Verwaltungsgesellschaft M.B.H.	03/21/2002	
B15	WO	02/26703		A1	Prolifix Limited	04/02/2002	
B16	WO	02/30879		A2	Prolifix Limited	04/18/2002	
B17	WO	02/46129		A2	Abbott Laboratories	06/13/2002	
B18	WO	02/51842		A1	F. Hoffmann-LaRoche AG	07/04/2002	
B19	WO	02/51846		A1	Lee et al.	07/04/2002	
B20	WO	02/74298		A1	Ono Pharmaceutical Co., Ltd.	09/26/2002	A
B21	WO	03/24448		A2	Methylgene, Inc.	03/27/2003	
B22	WO	2004/14899		A1	Smithkline Beecham Corporation	02/19/2004	

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.		T <sup>6</sup>
	B23	CLOSSE et al., "Isolierung und Strukturaufklärung von Chlamydoxin," Helvetica Chimica Acta, 1974, Vol. 57, No. 60-61, pp. 533-545.		none

Examiner Signature

Date Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

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Date Submitted: May 6, 2005

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Sheet

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## Complete if Known

Application Number	10/522,873
Filing Date	2/2/2005
First Named Inventor	Janet Ann ARCHER
Group Art Unit	Unassigned
Examiner Name	Unassigned
Attorney Docket Number	040283-0213

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	B24	DARKIN-RATTRAY et al., "Apicidin: A novel antiprotozoal agent that inhibits parasite histone deacetylase," Proc. Natl. Acad. Sci. USA, November 1996, Vol. 93, pp. 13143-13147.	
	B25	EL-DEEN et al., "Synthesis and investigation of mass spectra of 3-[5'-(2'-substituent)-thienyl]benzo[5,6]coumarins," Phosphorus, Sulfur, and Silicon, 2003, Vol. 178, pp. 1463-1476.	
	B26	GEFFKEN, "Thiophenisostere der Salicylohydroxamsäure," Pharmazie, 1993, Vol. 48, H.6, pp. 407-410.	none
	B27	HIROTA et al., "Mass Spectrometric Determination of Amino Acid Sequence in Cyl-2, a Novel Cyclotetrapeptide from <i>Cylindrocladium scoparium</i> ," Biomedical Mass Spectrometry, 1974, Vol. 1, pp. 15-19.	
	B28	JUNG et al., "Amide Analogues of Trichostatin A as Inhibitors of Histone Deacetylase and Inducers of Terminal Cell Differentiation," J. Med. Chem., 1999, Vol. 42, pp. 4669-4679.	
	B29	JUNG et al., "Analogues of Trichostatin A and Trapoxin B as Histone Deacetylase Inhibitors," Bioorganic & Medicinal Chemistry Letters, 1997, Vol. 7, No. 13, pp. 1655-1658.	
	B30	KIJIMA et al., "Trapoxin, an Antitumor Cyclic Tetrapeptide, Is an Irreversible Inhibitor of Mammalian Histone Deacetylase," The Journal of Biological Chemistry, October 25, 1993, Vol. 268, o. 30, pp. 22429-22435.	
	B31	KIM et al. "Oxamflatin is a novel antitumor compound that inhibits mammalian histone deacetylase," Oncogene, 1999, Vol. 18, pp. 2461-2470.	
	B32	MASSA et al., "3-(4-Aroyl-1H-pyrrol-2-yl)-N-hydroxy-2-propenamides, a New Class of Synthetic Histone Deacetylase Inhibitors," J. Med. Chem., 2001, Vol. 44, pp. 2069-2072.	
	B33	MAZUCCO et al., "Cell cycle regulation," American Association for Cancer Research, 93 <sup>rd</sup> Annual Meeting (Part V), April 6-10, 2002.	
	B34	RICHARDS et al., "Randomized, double-blind, placebo-controlled phase 2 study of the histone deacetylase inhibitor CI-994 plus gemcitabine (CI-994+G) versus placebo plus gemcitabine (P+G) in the treatment of patients with advanced pancreatic cancer (APC)," American Society of Clinical Oncology (ASCO), 2002 ASCO Annual Meeting, Abstract 644.	
	B35	SANDOR et al., "Phase I Trial of the Histone Deacetylase Inhibitor, Depsiteptide (FR901228, NSC 630176), in Patients with Refractory Neoplasms," Clinical Cancer Research, March 2002, Vol. 8, pp. 718-728.	
	B36	SCHMIDT et al., "Inhibitors of Histone Deacetylase Suppress the Growth of MCF-7 Breast Cancer Cells," Arch. Pharm. Pharm. Med. Chem., 1999, Vol. 332, No. 10, pp. 353-357.	
	B37	SHUTE et al., "Analogues of the Cytostatic and Antimitogenic Agents Chlamydocin and NC-Toxin: Synthesis and Biological Activity of Chloromethyl Ketone and Diazomethyl Ketone Functionalized Cyclic Tetrapeptides," J. Med. Chem., 1987, Vol. 30, pp. 71-78.	

Examiner Signature

Date Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 608. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

\*Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.<sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

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First Named Inventor	Janet Ann ARCHER
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Examiner Name	Unassigned

Attorney Docket Number 040283-0213

## NON PATENT LITERATURE DOCUMENTS

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	B38	SU et al., "A Novel Istone Deacetylase Inhibitor Identified by High-Throughput Transcriptional Screening of a Compound Library," <i>Cancer Research</i> , June 15, 2000, Vol. 60, pp. 3137-3142.	
	B39	UMEHARA et al., "Studies on WF-3161, A New Antitumor Antibiotic," <i>The Journal of Antibiotics</i> , May 1983, pp. 478-483.	
	B40	WATERHOUSE, "CA 19-9 levels in patients with advanced pancreatic cancer (APC) treated in a randomized, phase II trial with the histone deacetylase inhibitor CI-994 + gemcitabine (CI-994+G) versus placebo + gemcitabine (P+G)," <i>American Society of Clinical Oncology (ASCO), 2002 ASCO Annual Meeting</i> , Abstract 589.	
	B41	WILLIAMS, L. "Histone deacetylase inhibitors and other novel agents," <i>American Association for Cancer Research, 93<sup>rd</sup> Annual Meeting (Part II)</i> , April 6-10, 2002.	
	B42	YOSHIDA et al., "Potent and Specific Inhibition of Mammalian Histone Deacetylase Both <i>in Vivo</i> and <i>in Vitro</i> by Trichostatin A," <i>The Journal of Biological Chemistry</i> , October 5, 1990, Vol. 265, No. 28, pp. 17174-17179.	

Examiner Signature

Date Considered

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<sup>a</sup> Unique citation designation number. <sup>b</sup>See attached Kinds of U.S. Patent Documents. <sup>c</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>d</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>e</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>f</sup>Applicant is to place a check mark here if English language Translation is attached.

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